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Running head: EXERCISE POSTURE AND EXECUTIVE FUNCTION IN TIA

Acute effects of exercise posture on executive function in transient ischemic attack patients

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Abstract

In patients with stroke or transient ischaemic attacks (TIA), a decline in executive function may limit an individual's ability to process motor tasks and re-learn motor skills. The purpose of this study was to assess the acute effect of exercise posture (seated vs. supine cycle ergometry) on executive function and prefrontal cortex perfusion, in patients with TIA. Eleven TIA patients (65 ± 10 y) and 15 age-matched, healthy-controls (HC; 62 ± 7 y) completed two exercise tests to maximal capacity (1 x seated; 1 x supine) and two 30-minute sub-maximal exercise tests (1 x seated, 1 x supine). Executive function was assessed prior-to and following (1.5-min Post, 15-min Post) the submaximal exercise tests using a Stroop Task. Prefrontal cortex perfusion (total hemoglobin) was continuously recorded using near infrared spectroscopy. There was no Posture (seated, supine) by Group (TIA, HC) interaction for the Stroop task ($p > .05$). HC completed Stroop tasks significantly faster than TIA ($51.9[10.3]$ vs. $64.2[8.5]$ s, respectively); while Stroop completion time significantly improved between Baseline and 1.5-min Post ($61.3[10]$ vs. $58.1[9.4]$ s, respectively) and 1.5-min Post and 15-min Post ($54.8[8.9]$ s). Posture and Group had no significant influence on prefrontal cortex perfusion ($p > .05$). In conclusion, executive function improves to a similar extent in TIA and age-matched, healthy-controls following an acute bout of exercise, regardless of exercise posture. As acute improvements in executive function were maintained for 15 minutes, there could be an important

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1 window of opportunity for assigning executive tasks following exercise rehabilitation
2 for patients with TIA.

3 *Keywords:* stroke, cerebral perfusion, cognition, prefrontal cortex, supine, cycling

4

5

Introduction

Following a stroke many patients suffer from impaired mobility and are at risk of losing their independence. While physical rehabilitation is effective for restoring mobility, the speed and degree of restoration to normal function may be impeded by cognitive impairments (McKinney et al., 2002). In particular, a decline in executive function may limit the ability to process motor tasks and re-learn motor skills. These cognitive impairments result from infarcted brain tissue and subsequent hypoperfusion and hypo-oxygenation of the infarcted area and adjacent regions (Baron et al., 1981; Hillis et al., 2002, 2006). Indeed, the degree of hypoperfusion seems to correlate with the degree of cognitive dysfunction (Hillis, et al., 2002; Hillis et al., 2001), and restoration of perfusion has been demonstrated to improve cognitive performance in acute ischaemic stroke (Heiss et al., 1998; Hillis, Barker, Beauchamp, Gordon, & Wityk, 2000; Hillis, et al., 2006; Olivot et al., 2008). By way of logical extension, simple strategies which acutely improve cognitive function may enhance the rehabilitation process.

Exercise may be a simple, cost-effective and easily administered therapy for improving cerebral perfusion and cognitive function. A meta-analysis has identified a limited number of studies examining physical activity and cognition in stroke patients; while cognitive function was atypically the primary outcome measure, and the cognitive assessment tools were generally suboptimal, physical activity was shown to improve cognitive function (Cumming, Tyedin, Churilov, Morris, & Bernhardt, 2011). These findings are in-line with a number of randomized control

1 trials which have demonstrated that a single bout of aerobic exercise can acutely
2 improve various cognitive domains (Chang, Labban, Gapin, & Etnier, 2012),
3 including spatial and executive functioning (Colcombe & Kramer, 2003).

4 Consideration does need to be given to the prescribed exercise intensity and
5 modality. A meta-analysis reported that incremental exercise in healthy subjects
6 increased prefrontal cortex oxygenation in a quadratic manner, rising between
7 moderate and hard intensities, then falling at very hard intensities (Rooks, Thom,
8 McCully, & Dishman, 2010). In terms of exercise modality, owing to impaired motor
9 control in stroke patients, the safest form of aerobic exercise is considered to be cycle
10 ergometry. While upright cycling is most typically prescribed for these patients, we
11 recently reported that recumbent cycle ergometry in healthy young men acutely
12 increased prefrontal cortex oxygenation by a greater magnitude (Faulkner, Lambrick,
13 Kaufmann, & Stoner, 2016). This may be because recumbent exercise enhances
14 cardiac output (Quinn, Smith, Vroman, Kertzer, & Olney, 1995; Saitoh et al., 2005;
15 Walsh-Riddle & Blumenthal, 1989), and cardiac output has been shown to have a
16 linear relationship with cerebral blood flow (Ogoh & Ainslie, 2009). Contrary to the
17 hypothesis, executive function was found to improve by a similar amount for both
18 upright and recumbent exercise; however, there may be a ceiling effect in healthy
19 young men who would not be expected to have impaired executive function.

20 The current study recruited patients diagnosed with a transient ischaemic
21 attack (TIA), typically reported to be a minor form of stroke, and age-matched
22 healthy controls. TIA patients were recruited as, i) they could engage with 30 minutes

of moderate intensity cycling exercise in a seated and supine position, and ii) because recent studies investigating cognition after TIA suggest that deficits in executive function persist at least 7 days post-TIA (Ganzer, Barnes, Uphold & Jacobs, 2016). The purpose of this was to determine the effects of Group (TIA vs. control) and Posture (seated vs. supine) on, i) executive function and ii) prefrontal cortex perfusion. Four null hypotheses were tested, there is no relationship between: H1) Group and executive function; H2) Posture and executive function; H3) Group and prefrontal cortex perfusion; H4) Posture and prefrontal cortex perfusion. Accordingly, the researchers anticipated that executive function and prefrontal cortex perfusion would be greater in: i) the healthy age-matched control group than TIA group, and ii) during supine rather than seated exercise. Findings from this study may aid rehabilitation specialists in designing optimal rehabilitation strategies.

Method

Participants

Eleven TIA patients (age: 65.1 ± 10.1 y; height: 169.7 ± 11.3 cm; body mass: 85.8 ± 16.9 kg; 9 male, 2 female) and fifteen healthy age-matched controls (age: 61.5 ± 7.1 y; height: 176.6 ± 8.0 cm; body mass: 84.9 ± 16.3 kg; 13 male, 2 female) volunteered. The TIA participants were recruited within 7 ± 3 days of the event, and were diagnosed with a high risk TIA (ABCD² score ≥ 4), after review by a specialist stroke physician. The TIA participants completed an electrocardiogram (ECG) assessment to establish appropriate cardiovascular health for this study. Patients were

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excluded if they had any of the following: oxygen dependence, uncontrolled angina, unstable cardiac conditions (i.e., atrial fibrillation), uncontrolled diabetes mellitus, major medical conditions, claudication, febrile illness, significant cognitive impairment, immobile. Control group participants completed a coronary artery disease risk stratification assessment to ensure that they were asymptomatic of illness, disease or mental disability and free of any injury. Due to the nature of the assessment of executive function, participants were excluded if they suffered from colour blindness or attention deficits. This research was conducted in agreement with the guidelines and policies of the institutional ethics committee and New Zealand's health and disability ethics committee.

Procedures

Participants performed two familiarisation sessions and four laboratory-based exercise protocols on a cycle ergometer (Velotron, RacerMate, Seattle, U.S.A.), within a thermo-neutral environment. Tests were performed on either an upright, seated (1 x graded exercise test [GXT], 1 x 30 minute moderate intensity exercise bout) or a supine (1 x GXT, 1 x 30 minute moderate intensity exercise bout) cycle ergometer. Tests were performed in a semi-randomized order, separated by 48 to 72 hours, as it was necessary for moderate intensity exercise bouts to proceed the respective GXTs. To reduce the risk of anticipatory effects on physiological parameters, the display screen of the physiological markers (i.e., oxygen uptake [$\dot{V}O_2$], minute ventilation [\dot{V}_E], respiratory exchange ratio [RER], heart rate [HR]),

1 along with all cycle ergometer information (i.e., power output), was concealed from
2 the participant during each exercise test.

3 The Stroop task was used to assess executive function following 10-minutes
4 of quiet, supine rest (Baseline), and 1.5- (1.5-min Post) and 15-minutes (15-min Post)
5 following the completion of each moderate intensity exercise bout. Pre-frontal cortex
6 perfusion was monitored continuously and in real-time, using near-infrared
7 spectroscopy (Artinis Medical Systems BV, Zetten, The Netherlands), throughout the
8 Stroop tasks and exercise protocols (Figure 1). Respiratory variables were
9 continuously recorded throughout each moderate intensity exercise bout, and the
10 participant's blood pressure, heart rate (HR) and ratings of perceived exertion (RPE;
11 Borg, 1998) were recorded every 10 minutes during exercise.

13 **Seated and supine GXT to maximal functional capacity**

14 The GXTs were used to determine the exercise intensities that would be
15 prescribed in both the seated and supine submaximal exercise tests. The seated and
16 supine GXTs were continuous and incremental, commenced at 60 W and increased 12
17 W per minute. Criteria for termination of the maximal GXT was primarily based on
18 volitional exhaustion, although two or more of the following secondary criteria were
19 accepted as indicators of maximal functional capacity: HR within 10 beats/min of
20 age-predicted maximum, $\text{RER} \geq 1.10$ or $\text{RPE} \geq 18$ on completion of the tests (ACSM,
21 2013). On-line respiratory gas analysis was performed using a breath-by-breath
22 automatic gas exchange system (Sensormedics Corporation, Yorba Linda, CA, USA),

following volume and gas calibration. Heart rate was monitored using a wireless chest strap telemetry system (Polar Electro T31, Kempele, Finland). The Borg 6-20 RPE scale was used to quantify the subjective perception of effort every 3 minutes during the GXTs. Participants' peak oxygen consumption ($\dot{V}O_{2peak}$) and gaseous exchange threshold (GET) were ascertained for both exercise bouts.

Seated and supine submaximal exercise tests

During these tests participants cycled at a power output equivalent to GET for 30 minutes. The GET typically equates to a moderate exercise intensity (45-60% $\dot{V}O_{2max}$) (Seiler & Tønnessen, 2009). The V-slope method was used to analyse the slopes of $\dot{V}O_2$ and carbon dioxide ($\dot{V}CO_2$) volume curves from both the seated and supine GXTs to determine each participant's power output at GET (Beaver, Wasserman, & Whipp, 1986). Three independent researchers verified the interpretation of GET and the corresponding power outputs. Physiological markers were continuously monitored throughout the test.

Executive Function

Executive function was assessed using the Stroop task (Xavier Educational Software Ltd., Bangor, Wales), a classic measure of prefrontal cortex function which has been widely used to assess the effects of acute exercise on cognition (Hogervorst et al., 2008; Lucas et al., 2012; MacLeod, 1991; Vasques, Moraes, Silveira, Deslandes, & Laks, 2011). Participants were habituated with the Stroop task during

two familiarisation sessions, as well as following each GXT. In this study, the Stroop interference task was administered as it is more sensitive to executive function than the traditional Stroop word task (Durgin, 2000). Participants completed the Stroop interference task wherein four words ('blue', 'yellow', 'green', 'red') were randomly presented, consecutively, on a computer screen. The colour each word was presented in was either congruent or incongruent with the relevant semantic information (e.g., 'red' presented in the colour red or the colour green, respectively). Participants were tasked with identifying the colour of each word being presented as quickly as possible, responding by clicking on the respective answer button (blue, yellow, green, red). Each presentation of a word constituted a sequence; each test comprised 36 sequences. The total time to complete the test (completion time), average time per response (reaction time), and number of correct answers (response accuracy) were recorded as measures of performance (Baseline, 1.5-min Post, 15-min Post). Although a time-control (no exercise) condition was not included in the study design, unpublished findings from our laboratory has demonstrated good reliability when assessing Stroop performance before and after 30 minutes quiet seated rest in a young, healthy population. Similar findings have generally been shown for Near-infrared Spectroscopy (NIRS) measures (Supplementary Table A).

Near-infrared spectroscopy

Near infrared spectroscopy assessments have been demonstrated to provide a metric of cognitive activation similar to functional magnetic resonance imaging

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1 during cognitive performance tasks (Cui, Bray, Bryant, Glover, & Reiss, 2011). A
2 continuous wave NIRS device (PortaLite, Artinis Medical Systems BV, the
3 Netherlands), which emits infrared light at wavelengths of 760 and 850 nm, was used
4 to detect relative changes in concentrations of oxygenated hemoglobin [O₂Hb] and
5 deoxygenated hemoglobin [HHb], respectively, as well as the main parameter of
6 interest: total blood volume (tHb = [O₂Hb + HHb]), before, during and after the 30-
7 minutes of upright and supine exercise (Figure 1). Both wavelengths were emitted
8 from three transmitters at 3.0, 3.5, and 4.0 cm from the photo diode detector, allowing
9 for theoretical penetration distances between 1.5-2 cm (Chance, Dait, Zhang,
10 Hamaoka, & Hagerman, 1992). Data was collected at 10 Hz, and a differential path-
11 length factor of 4.0 was used to correct for photon scattering within the tissue
12 (Ferrari, Wei, Carraresi, De Blasi, & Zaccanti, 1992). Depending on individual head
13 geometry, the probe was positioned over the participant's prefrontal cortex at Fp1 for
14 right sided dominant participants and at Fp2 for left sided dominant participants
15 according to the International 10-20 system of Electrode Placement (Klem, Luders,
16 Jasper, & Elders, 1999). For the TIA participants, the NIRS probe was placed on the
17 side in which their TIA event occurred. The effect of ambient light on NIRS was
18 reduced by conducting all exercise tests and Stroop tasks in a dimly lit laboratory.
19 The NIRS device was fixed to the skin with bi-adhesive tape and covered with a dark
20 opaque cloth to prevent signal contamination by ambient light, as per manufacturer
21 recommendations.

22 INSERT FIGURE 1 ABOUT HERE

1

2 **Data Analysis**

3 Statistical analyses were performed using Statistical Package for Social
4 Sciences version 21 (SPSS, Inc., Chicago, Illinois, USA). All data are reported as
5 means (standard deviation, SD) or mean differences (95% confidence intervals [CI]),
6 unless otherwise specified. For all statistical tests, alpha was set at 0.05 with an
7 adjustment made via the Bonferroni technique to protect against type 1 error. Effect
8 size are represented using partial eta squared (η_p^2), with 0.0099, 0.0588, and 0.1379
9 representing a small, medium, and large effect (Cohen, 1988).

10 *H1 and H2:* Independent *t*-tests were used to compare Stroop task performance
11 at Baseline between TIA and healthy-control (HC) participants for both seated and
12 supine exercise. A repeated-measures ANOVA: Group (TIA vs. HC) by Posture
13 (Seated vs. Supine) by Time (Baseline, 1.5-min Post, 15-min Post), was used to
14 assess the rate of change in Stroop task performance (time taken and number of
15 correct answers). Where assumptions of sphericity were violated, the critical value of
16 *F* was adjusted by the Greenhouse–Geisser epsilon value from the Mauchley Test of
17 Sphericity. Where significant differences were identified, post-hoc analysis using
18 dependent *t*-tests were performed.

19 *H3 and H4:* Changes in primary (tHb) and secondary (O₂Hb, HHb) NIRS
20 markers were analysed using a repeated-measures ANOVA, as above. Regression
21 analysis was used to assess whether the change in tHb, O₂Hb and HHb (independent

variables [IV]) (Baseline to 1.5-min Post) accounted for a significant amount of variance in the change in Stroop performance scores (dependent variable [DV]).

Results

There were no differences in demographic characteristics between TIA and HC participants (all $p > .05$; Table 1). The diagnostic location of the 11 TIA patients were as follows; Anterior circulation ($n = 7$), posterior circulation ($n = 3$), uncertain territory ($n = 1$).

INSERT TABLE 1 ABOUT HERE

Graded Exercise Test and Submaximal Exercise Test

There were no Posture by Group interaction effects for any GXT or GET variables (all $p > .05$; Table 2). Significant Posture main effects were observed for $\dot{V}O_{2peak}$ (mean difference [95 %CI]; 2.0 [0.4 to 3.7] mL·Kg⁻¹·min⁻¹), HR (mean difference [95 %CI]; 11 [8 to 14] b·min⁻¹) and power output (mean difference [95 %CI]; 21 [15 to 28] W) on completion of the GXTs (all $p < .05$), with higher values reported during the seated GXT compared to the supine GXT. A Group main effect was also observed for $\dot{V}O_{2peak}$ ($p < 0.05$), with higher values reported for HC compared to TIA (mean difference [95 % CI]; 8.6 [1.1 to 16.0] mL·Kg⁻¹·min⁻¹). At GET, despite differences in absolute $\dot{V}O_2$ and power output between Posture and Group ($p < .05$), when expressed as a proportion of peak values, there were no differences in $\dot{V}O_2$ or power output for Posture or Group ($p > .05$; Table 2). Similar

findings were observed for other physiological (minute ventilation, respiratory exchange ratio, heart rate) and perceptual responses at the end of the seated and supine submaximal exercise tests ($p > .05$; Supplementary Table B).

INSERT TABLE 2 ABOUT HERE

H1 and H2: Executive Function

There were no Posture by Group by Time interactions for Stroop completion time or the number of correct answers ($p > .05$; Table 3). Across groups, Stroop completion time significantly improved between Baseline and 1.5-min Post (61.3 [10] vs. 58.1 [9.4] s, respectively) and 1.5-min Post and 15-min Post (54.8 [8.9] s). There was a significant Group (H2) main effect, with HC completing the Stroop task significantly faster than TIA (51.9 [10.3] vs. 64.2 [8.5] s, respectively; mean difference [95 % CI]; 12.3 [4.9 to 19.8] s). There was no Posture (H1) main effect ($p > .05$).

INSERT TABLE 3 ABOUT HERE

H3 and H4: Prefrontal Cortex Perfusion

There was no Posture by Group by Time interaction, or Group (H3) or Posture (H4) main effects for each NIRS measure (all $p > .05$). Time main effects were observed for tHb, O₂Hb, and HHb ($p < 0.001$; η_p^2 all 0.81 – 0.90; Figure 2). Post-hoc analysis demonstrated significant increases in these measures between Baseline and

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1 1.5-min Post (mean difference [95 % CI], tHb 15.9 [12.4 to 19.3] %; O₂Hb 14.4 [11.3
2 to 17.5] %; HHb 1.5 [0.9 to 2.1] %).

3 INSERT FIGURE 2 ABOUT HERE

4 5 **Prefrontal Cortex Perfusion and Executive Function**

6 As there were no between Group differences for prefrontal cortex perfusion,
7 regression analysis was implemented with the entire sample (TIA + HC). Neither tHb
8 ($p > .05$; $R^2 = 0$; beta [standardized coefficient] = -.07; Standard error = 0.126; beta
9 [unstandardized coefficient] = -0.06), O₂Hb ($p > .05$; $R^2 = 0$; beta [standardized
10 coefficient] = -0.06; Standard error = 0.09; beta [unstandardized coefficient] = -0.04)
11 or HHb ($p > .05$; $R^2 = .03$; beta [standardized coefficient] = -0.18; Standard error =
12 0.20; beta [unstandardized coefficient] = -0.24) explained a significant amount of the
13 variance in the change in Stroop task performance (Baseline to 1.5-min Post; all $p >$
14 0.05).

15 **Discussion**

16 Findings from this study show that TIA patients have a lower baseline
17 executive function than age-matched healthy controls, but executive function
18 improves similarly for both Groups following exercise, and these benefits are
19 maintained for at least 15-minutes. However, exercise Posture (seated, supine) does
20 not influence the improvement in executive function. Further, cerebral perfusion was
21 shown to improve irrespective of Group (TIA, control) or Posture. These novel

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findings support the use of exercise to improve executive function, which may in-turn improve rehabilitation practice.

Executive Function

For the present study, the hypothesis that Group would effect executive function was rejected (H1), while the hypothesis that Posture will effect executive function (H2) was not rejected. The Group main effect can be attributed to baseline differences (Table 3), as the relative improvement in executive function 15-minutes post-exercise was similar for both TIA and controls (10.5 vs. 10.6 %, respectively). While changes in executive function following moderate intensity exercise have been shown previously in various populations (Chang, et al., 2012; Lambourne & Tomporowski, 2010; McMorris, Sproule, Turner, & Hale, 2011; Tomporowski, 2003), to our knowledge, this is the first study to demonstrate that acute exercise improves executive function in TIA patients, and that these patients respond similarly to healthy, age-matched individuals.

The current study explored the association between Posture and executive function (H2) following a recent study from our group, which demonstrated that, compared to seated cycle ergometry, recumbent cycle ergometry in healthy young men acutely increased prefrontal cortex oxygenation by a greater magnitude (Faulkner, et al., 2016). The failure to reject H2 may be attributable to the lack of effect of Posture on cerebral perfusion (tHb) in the current study, or the lack of direct association between cerebral perfusion and executive function, both of which are discussed below.

1

2 **Prefrontal Cerebral Perfusion**

3 In this study we used tHb as a measure of prefrontal cortex perfusion, and
4 found that moderate exercise intensity (~52 % of $\dot{V}O_{2peak}$) increased perfusion by 15
5 u/mol. However, the increase in perfusion was not influenced by either Group (H3)
6 or Posture (H4). As previously mentioned, the failure to reject H4 is contrary to a
7 recent study by our group (Faulkner, et al., 2016). This may, at least in part, be
8 explained by the wide variation in prefrontal cortex perfusion (tHb) and oxygenation
9 (O_2Hb) responses to exercise for participants in the current study (Figure 2), whereas
10 for our previous study the responses were fairly consistent between participants. This
11 variation may be explained by differences in the respective cohorts; the previous
12 study recruited a young (24.6 ± 4.3 y), healthy and physically-active homogenous
13 population.

14 Regression analysis demonstrated that, regardless of Posture or Group, the
15 NIRS markers (tHb, O_2Hb , HHb) did not explain a significant portion of the variance
16 for change in executive function. This is contrary to a previous study by Endo et al.
17 (2013) who found that, following arm ergometry at 40% maximal functional capacity
18 (but not at 20 or 60 % of maximal capacity), improvements in oxygenation to the
19 prefrontal cortex correlated with improved executive function (Stroop). The contrary
20 findings may be explained by the heterogeneous responses for the participants in the
21 current study, or may suggest that other mechanism/s contributed to the observed
22 exercise-induced improvements in executive function. It has been suggested that the

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exercise-induced up-regulation of neurotransmitters such as dopamine, serotonin, norepinephrine and endorphine (Barenberg, 2012; Best, 2010; Meeusen, Watson, Hasegawa, Roelands, & Piacentini, 2006), as well as brain-derived neurotropic factor (Saucedo Marquez, Vanaudenaerde, Troosters, & Wenderoth, 2015) play a crucial role in improving executive function (Barenberg, 2012; Robbins & Arnsten, 2009).

Clinical implications

These findings may have important implications for rehabilitation of TIA and stroke patients. Previously, recumbent/supine cycling exercise has been suggested to be a safer alternative to upright/seated cycling, and may provide practical advantages for muscle and aerobic training in patients with impaired physical function (Gregor et al., 2002; Kerr, Rafferty, Moffat, & Morlan, 2007). In the present study, a similar level of improvement was observed in executive function between the two body positions. This may be due to the fact that participants were exercising at a similar proportion of their maximal functional capacity at the end of both (seated and supine) exercise tests (see Table 2 and Supplementary Table B). Participants were also exercising at a similar perception of exertion during the seated and supine exercise, at approximately a 'somewhat hard' to 'hard' perception of exertion according to the Borg 6-20 RPE Scale. Although both exercise modes and the prescribed exercise intensity could be useful in the rehabilitation setting, supine exercise may be deemed more appropriate as it may be a safer exercise modality for those populations who lack mobility.

In our study, continued improvements in Stroop performance were observed 15 minutes after exercise cessation (Table 3). This is in support of the findings of Chang and colleagues' (2012), whose meta-analysis found that the greatest positive effect on cognition occurs 11-20 minutes after exercise cessation. More recent research has shown that improvements in cognition can be maintained for a period of at least 30 minutes post-exercise (Lambrick, Stoner, Grigg, & Faulkner, 2016; Peiffer, Darby, Fullenkamp, & Morgan, 2015; Tsukamoto et al., 2016). These previous findings, together with the current findings, may have practical implications for the rehabilitation environment. Following moderate-intensity exercise there may be a window of opportunity for presenting patients with neurological deficit with tasks that challenge executive function.

Future considerations

To determine the mechanistic link between acute exercise and executive function, studies with larger sample size are required, and which simultaneously record cerebral perfusion, neurotransmitters and psychological factors (arousal, mood state). Understanding the mechanism(s) of action will enable the identification of the optimal exercise paradigm for enhancing executive function. For example, while moderate intensity exercise is most effective for increasing cerebral blood flow (Ogoh & Ainslie, 2009), high-intensity intermittent exercise may elicit greater elevations in serum BDNF (Saucedo Marquez, et al., 2015). Furthermore, compared to continuous and moderate intensity exercise, short periods of intense exercise have been shown to

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1 result in greater elevations of BDNF and peripheral catecholamines, and can improve
2 vocabulary learning by 20% in just one week (Winter et al., 2007). Although this may
3 be evident, the severity and location of the stroke may have a significant impact on
4 the use of exercise in improving executive function, as some stroke survivors may be
5 unable to exercise at low, moderate or high intensities, or for prolonged durations
6 (i.e., 30 minutes of submaximal exercise). It would also be useful if future research
7 investigated the effect of exercise on executive function in a homogenous sample of
8 stroke patients. From a clinical/rehabilitation perspective, besides determining the
9 optimal exercise prescription, further research is needed to determine the optimal
10 timing post-exercise for assigning tasks that challenge executive function.
11 Additionally, when undertaking such research investigations into the utility of
12 exercise for improving cognition or cerebral perfusion, it would also be beneficial to
13 include a time-control condition.

14
15 In conclusion, the present study has demonstrated that an acute bout of moderate
16 intensity exercise improves executive function in TIA patients, and that TIA patients
17 appear to respond similarly to healthy, age-matched controls. The improvements were
18 not moderated by exercise Posture (seated vs. supine), and were not associated with
19 prefrontal cortex perfusion. Importantly, the improvements in executive function
20 were maintained for 15 minutes, suggesting that there could be an important window
21 for assigning tasks that challenge executive function.

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9 **Figure Legends**

10 **Figure 1:** Example of total hemoglobin (tHb), oxyhemoglobin (O₂Hb) and
11 deoxyhemoglobin (HHb) before, during and following the upright exercise protocol.

12 A – Baseline rest; B – Baseline Stroop task; C – 30-minutes of upright exercise; D –
13 1.5-minutes Post-exercise Stroop task; E – 15-minutes Post-exercise Stroop task.

14

15 **Figure 2:** Absolute change (mean, SD) in tHb, O₂Hb and HHb at each baseline (rest)
16 and each Stroop task assessment time point (Baseline, 1.5-min Post, 15-min Post).

17 Significant Time effect: $p < 0.05$ vs. Baseline Stroop.

18

1 **Table 1:** Mean (SD) participant demographics

	TIA	HC	Mean Diff	95 % CI	P value
Age (y)	65 (10)	61 (7)	3.64	-3.6 to 10.9	0.310
Weight (kg)	86 (17)	85 (16)	0.95	-13.5 to 15.4	0.893
Height (m)	1.70 (0.10)	1.71 (0.08)	-0.01	-0.1 to 0.1	0.096
BMI (kg·m ²)	29.8 (7.1)	27.2 (3.9)	2.56	2.2 to -2.0	0.260
BF (%)	33 (12)	26 (8)	7.49	4.0 to -1.0	0.080
SBP (mmHg)	133 (16)	133 (24)	0.44	9.0 to -18.3	0.961
DBP (mmHg)	79 (5)	76 (5)	2.93	2.2 to -1.6	0.195
RHR (b·min ⁻¹)	59 (9)	59 (7)	0.58	3.2 to -6.0	0.857

2

3 *Abbreviations:* CI = Confidence interval; BMI = Body mass index; BF = Body Fat;
4 SBP = Systolic blood pressure; DBP = Diastolic blood pressure; RHR = Resting heart
5 rate.

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1 **Table 2:** Mean (SD) data reported on completion of the GXT and at GET for both Groups (TIA, HC) and Posture (seated, supine). Effect

		Posture by Group Interaction									Group main effect					Posture main effect				
		TIA				HC					TIA		HC			Seated		Supine		
		Seated		Supine		Seated		Supine			Total		Total			Total		Total		
		X	SD	X	SD	X	SD	X	SD	η_p^2	X	SD	X	SD	η_p^2	X	SD	X	SD	η_p^2
GXT	$\dot{V}O_{2max}(mL \cdot kg^{-1} \cdot min^{-1})$	28.2	(7.7)	28.5	(8.6)	39.1	(8.9)	34.8	(8.9)	0.27	28.4	(9)	36.9*	(8.6)	0.22	33.6	(8.7)	31.7*	(9.3)	0.20
	$\dot{V}O_{2max} (L \cdot min^{-1})$	2.4	(0.6)	2.4	(0.8)	3.2	(0.6)	2.9	(0.6)	0.26	2.4	(0.6)	3.1	(0.6)	0.23	2.8	(0.7)	2.6	(0.7)	0.23
	RER	1.1	(0.1)	1.1	(0.1)	1.1	(0.1)	1.1	(0.1)	0.04	1.1	(0.1)	1.1	(0.1)	0.03	1.1	(0.1)	1.1	(0.1)	0.00
	HR (b·min ⁻¹)	149	(20)	141	(23)	160	(11)	147	(10)	0.16	145	(15)	153	(15)	0.07	154	(16)	144*	(16)	0.70
	RPE	17	(2)	17	(2)	18	(1.4)	18	(1)	0.02	17	(1.5)	18	(2)	0.09	18	(2)	18	(2)	0.04
	PO (W)	161	(34)	149	(44)	205	(49)	173	(41)	0.33	155	(43)	189	(43)	0.14	182	(48)	161*	(45)	0.69
GET	$\dot{V}O_2 (L \cdot min^{-1})$	1.2	(0.5)	1.3	(0.4)	1.8	(0.4)	1.5	(0.4)	0.29	1.3	(0.4)	1.7*	(0.4)	0.21	1.5	(0.5)	1.4*	(0.4)	0.21
	$\dot{V}O_2 (\%)$	52	(12)	54	(7)	56	(7)	53	(9)	0.06	53	(7)	55	(7)	0.02	54	(9)	53	(8)	0.00
	PO (W)	87	(19)	81	(26)	109	(30)	91	(20)	0.09	84	(23)	100*	(23)	0.11	98	(29)	86*	(24)	0.31
	PO (%)	55	(8)	54	(6)	53	(5)	54	(8)	0.01	55	(6)	53	(6)	0.02	54	(7)	54	(8)	0.00

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- 1 sizes are also reported (η_p^2)
- 2 *Significant Group or Posture main effect ($P < .05$)
- 3 *Abbreviations:* HR, heart rate; PO, power output; RER. Respiratory exchange ratio; RPE, ratings of perceived exertion

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1 **Table 3:** Mean (SD) Stroop completion time at baseline, Post and 15-min Post for Posture (Seated, Supine) and Group (TIA, HC)

			Seated			Supine			Seated + Supine		
			Baseline	Post	15-min	Baseline	Post	15-min	Baseline	Post	15-min
			Post			Post			Post		
Time	TIA	X	67.2	65.0	59.4	67.4	65.2	61.1	67.3	65.1	60.3
		SD	11.2	10.6	11.8	14.8	13.6	8.9	9.7	9.1	8.7
	HC	X	53.5	51.1	50.1	56.9	51.1	48.5	55.2	51.1	49.3
		SD	6.5	7.7	8.2	9.6	8.4	8.4	9.3	8.8	8.4
#Correct	TIA	X	36.0	36.0	35.9	36.0	35.3	36	36.0	35.7	35.9
		SD	0	0	0.3	0	1.4	0	0	0.5	0.3
	HC	X	36.0	35.8	35.9	35.8	36.0	35.9	35.9	35.9	35.8
		SD	0	0.6	0.5	0.6	0	0.5	0.2	0.4	0.3

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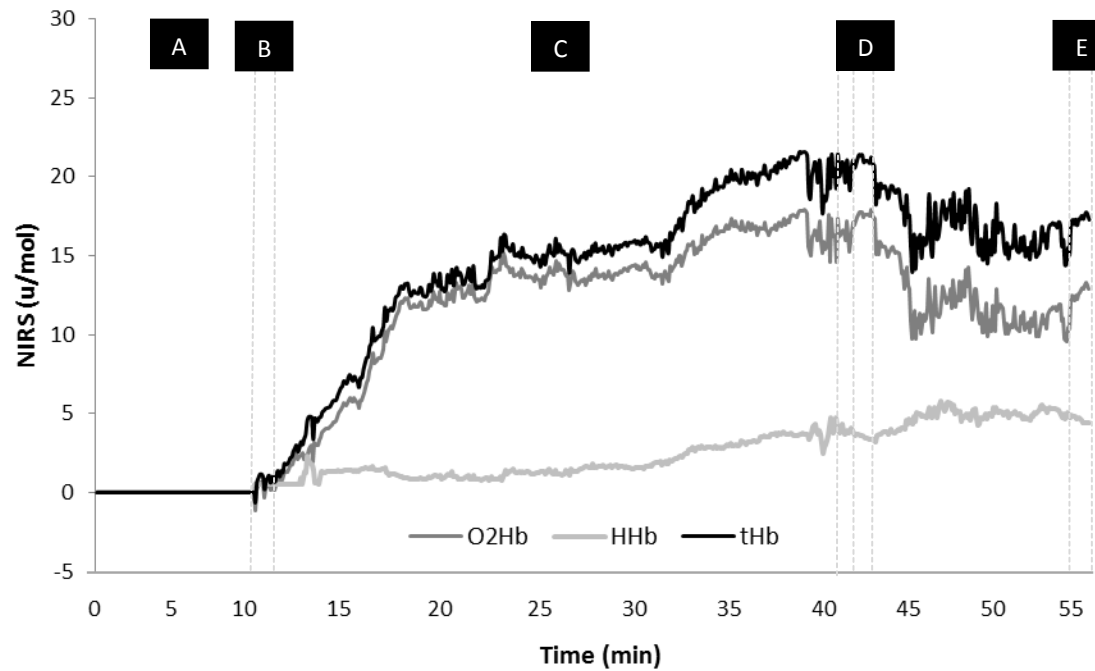


Figure 1: Example of total hemoglobin (tHb), oxyhemoglobin (O₂Hb) and deoxyhemoglobin (HHb) before, during and following the upright exercise protocol. A – Baseline rest; B – Baseline Stroop task; C – 30-minutes of upright exercise; D – 1.5-minutes Post-exercise Stroop task; E – 15-minutes Post-exercise Stroop task.

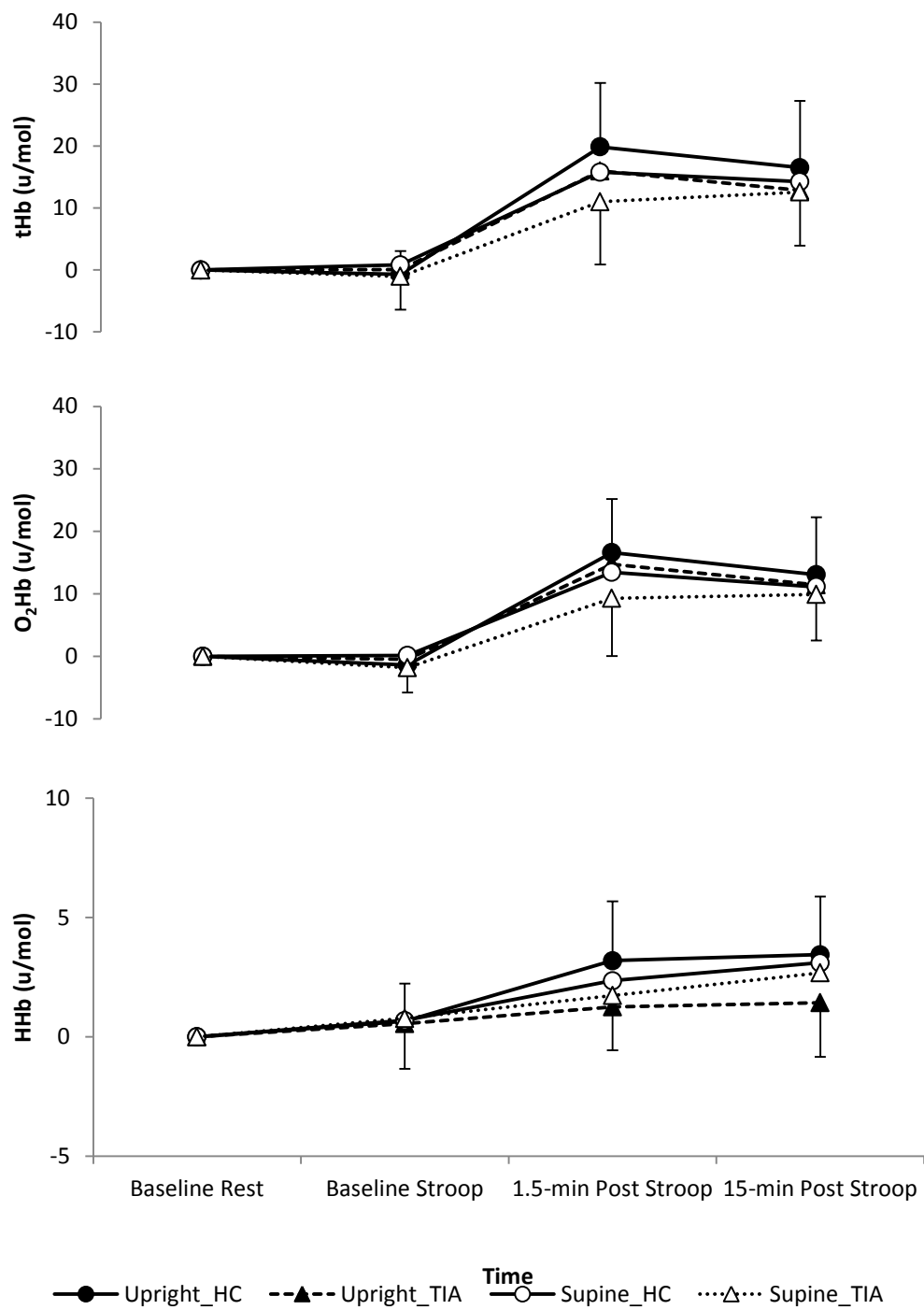


Figure 2: Absolute change (mean, SD) in tHb, O₂Hb and HHb at each baseline (rest) and each Stroop task assessment time point (Baseline, 1.5-min Post, 15-min Post). Significant Time effect: $p < 0.05$ vs. Baseline Stroop.

Supplementary Table A: Unpublished findings of the reliability of Stroop performance and NIRS measures before and after 30 minutes quiet seated rest (time-control condition), in a young healthy population.

Measure		ICC	SEM	CV (%)
Stroop*	Correct answers	0.90	0.13	1
	Total time	0.94	0.32	4
NIRS [#]	O ₂ Hb	0.95	0.27	6
	HHb	0.92	0.23	8
	tHb	0.95	0.29	5

Abbreviations: CV, Coefficient of variation; ICC, intra-class correlation coefficient; SEM, Standard error of the mean

*Stroop data was recorded following two familiarisation sessions. Both familiarisation sessions incorporated 2 x 36 presentations. Each presentation comprised 36 sequences. The data presented above is also based on the presentation of 36 sequences.

[#]The wider CV for NIRS is most likely due to: i) the sensitivity of the NIRS optodes to any form of movement, and ii) due to the inter-individual variation in blood flow to the cerebral cortex.

Supplementary Table B: Mean (SD) data of additional physiological and perceptual responses reported on completion of the 30 minute submaximal exercise tests for both Groups (TIA, HC) and Postures (seated, supine). Values are also presented as a proportion (%) of their maximal values ascertained from the GXT. Effect sizes are reported (η_p^2).

	Group main effect					Posture main effect				
	TIA		HC			Seated		Supine		
	X	SD	X	SD	η_p^2	X	SD	X	SD	η_p^2
V_E (L·min⁻¹)	47	(12)	58	(16)	0.12*	57	(14)	51	(13)	0.04
V_E (%)	54	(8)	56	(7)		55	(7)	55	(8)	
RER	0.9	(0.0)	0.9	(0.0)	0.01	0.9	(0.0)	0.9	(0.0)	0.01
RER (%)	81	(9)	83	(8)		82	(9)	82	(8)	
HR (b·min⁻¹)	122	(15)	129	(15)	0.05	134	(12)	120	(12)	0.26*
HR (%)	85	(9)	85	(11)		86	(9)	83	(10)	
RPE	13.4	(1.5)	13.8	(2.0)	0.01	13.5	(1.7)	14.0	(1.7)	0.02
RPE (%)	78	(12)	79	(14)		76	(12)	79	(13)	

*Significant difference in absolute values between Groups or Postures ($P < .05$)

Abbreviations: HR, heart rate, RPE, ratings of perceived exertion; V_E, minute ventilation; RER, respiratory exchange ratio